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EXAMINER KERR, KATHLEEN M				
ART UNIT		PAPER NUMBER		
1652				

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Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

10/017,324

Applicant(s)

WALSH ET AL.

Examiner

Kathleen M Kerr

Art Unit

1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 03 November 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-59 is/are pending in the application.
- 4a) Of the above claim(s) 56-58 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-55 and 59 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.  
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

### Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 7/30/02.
- 4) ☐ Interview Summary (PTO-413) Paper No(s) \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

## **DETAILED ACTION**

### ***Application Status***

1. In response to the previous Office action, a written restriction requirement (mailed on October 3, 2003), Applicants filed an election received on November 11, 2003. Claims 1-59 are pending in the instant Office action.

### ***Election***

2. Applicants' election of Group I, Claims 1-55 and 59, received on November 3, 2003 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (M.P.E.P. § 818.03(a)). Claims 56-58 are withdrawn from consideration as non-elected inventions. Claims 1-55 and 59 will be examined herein.

With respect to the election of species, since no prior art can be found using the elected species of ester (as opposed to thioester) substrates for TE domains, all the claims in the elected genus will be examined.

### ***Priority***

3. The instant application is granted the benefit of priority for the U.S. Provisional Application Nos. 60/256,596 and 60/332,763 filed on December 18, 2000 and November 6, 2001, respectively, as requested in the declaration and the first lines of the specification.

***Information Disclosure Statement***

4. The information disclosure statement filed on July 30, 2002 has been reviewed, and its references have been considered as shown by the Examiner's initials next to each citation on the attached copy.

***Objections to the Specification***

5. In the specification, the Abstract is objected to for not completely describing the disclosed subject matter (see M.P.E.P. § 608.01(b)). It is noted that in many databases and in foreign countries, the Abstract is crucial in defining the disclosed subject matter, thus, its completeness is essential. The Examiner suggests the inclusion of the full name of the enzymes, PKS or polyketide synthase and NRPS or non-ribosomal peptide synthetase, for completeness. Correction is required.

6. The specification is objected to for a typographical error. On page 45, in the middle of the page, the words "syntetase" and "uilt" are misspelled; the correct spellings are ---synthetase-- - and ---built--- as found elsewhere in the specification and the art. Correction is required.

7. In the specification on page 45, middle of the page, the description of the elongation/cyclization method depicted in Figure 3c is confusing. As described above this section, the PCP protein domain facilitates the dimerization of the substrates since one substrate is attached to the PCP domain and one to the TE domain (see Figure 3b). In the "excised" version, no PCP domain is present so it is unclear how dimerization is occurring. Clarification is required.

Art Unit: 1652

8. In the specification on page 46, bottom of the page, the description of methods using thioester substrates wherein one or more of the amide linkages between residues has been placed with ester linkages implies that data was collected ("similar to the rate observed for the substrate in Example 3"), but none is actually mentioned. Were these experiments actually performed with compounds 22-24? If so, the phrase ---data not shown--- should be present to clearly represent that the experiments have been performed. For compounds 22-23, it is not clear which TE domain was used if experiments were actually performed; compound 24 notes using the TycC TE domain. Again, this issue of compounds 25-26 on pages 47-48; compounds 25-26 note using the TycC TE domain. This "data not shown" issue is also a problem for compounds 27-28 on page 49. Clarification is required so the Examiner can effectively assess which experiments were performed and their data for issues of enablement and/or written description.

#### ***Objections to the Claims***

9. Claim 18 is objected to because of the following informalities: the claim consists of two sentences – all claims must be a single sentence ending in a period. Appropriate correction is required. The Examiner suggests an appropriate "wherein" clause for the second sentence.

10. Claim 48 is objected to for containing a typographical error in claim dependence. Claim 48, written as depending from Claim 46, which lacks any reference to  $R_1$ , further limits the identity of  $R_1$ , which can be found in Claim 47. Thus, Claim 48 reasonably should depend from Claim 47 and will be examined as such herein. Correction is required.

Art Unit: 1652

11. Claim 54 is objected to under 37 C.F.R. § 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. In the parent claim, Claim 50,  $n \geq 5$  but in Claim 54,  $n$  is between 1 and about 5 (i.e., less than 5 in some instances). Thus, Claim 54 attempts to alter the scope of Claim 50.

***Claim Rejections - 35 U.S.C. § 112***

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 1-55 and 59 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In Claim 1, the abbreviation "TE" is used without definition upon its first appearance. The Examiner suggests, in the first occurrence of the term, ---thioesterase (TE) domain protein--- for clarity. Correction is required.

13. Claims 4 and 37 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term "weakly-nucleophilic" is unclear. The term "weakly-nucleophilic" is a relative term that renders the claim indefinite. The term "weakly-nucleophilic" is not defined by the claim, the specification does not provide a standard for

Art Unit: 1652

ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably appraised of the scope of the invention.

14. Claims 6-8 and 39-41 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In the limitations of the pH, the phrases like “about 5” and “about 7” are unclear as to their scope. Does “about” limit to  $\pm 1$  pH unit? Or  $\pm 2$  pH units? Or  $\pm 5$  pH units? The specification used only a single pH, pH 7.0 (see page 40, Example 2), in the experiments. Thus, the ordinarily skilled artisan cannot ascertain the scope of the claims from any variability in the examples. The metes and bounds are not clear in the claims, and the specification does not aid in the interpretation of the term “about”. Clarification is required.

15. Claims 10, 12-33, and 59 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term “hydrocarbon” in Claims 10, 12, 18, and 59 is unclear because the definition in the specification on page 16 is repugnant to that known in the art wherein a hydrocarbon is limited to molecules containing only carbon and hydrogen atoms (see Stedman’s Dictionary). Where applicant acts as his or her own lexicographer to specifically define a term of a claim contrary to its ordinary meaning, the written description must clearly redefine the claim term and set forth the uncommon definition so as to put one reasonably skilled in the art on notice that the applicant intended to so redefine that claim term. *Process Control Corp. v. HydReclaim Corp.*, 190 F.3d 1350, 1357, 52 USPQ2d 1029, 1033 (Fed. Cir. 1999). Clarification is required.

Art Unit: 1652

16. Claim 10 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In the description of the linker, Claim 10 describes linking the thioester and the nucleophile; however, the formula in the claim contains an ester, not a thioester. Clarification is required.

17. Claims 10, 28-33 and 54 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In the limitations of the LINKER, the R group, z, and the sum of " $z+3m+3n$ ", the phrases like "about 4 carbon atoms" and "about 10 heteroatoms" are unclear as to their scope. Does "about" limit to  $\pm 1$  atom? Or  $\pm 2$  atoms? Or  $\pm 5$  atoms? The specification is replete with examples of highly varied substrates with various numbers of carbon atoms. Thus, the metes and bounds are not clear in the claims, and the specification does not aid in the interpretation of the term "about" as it applies in Claims 10 and 28. Clarification is required.

18. Claims 12-33 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In Claims 14 and 22, the compound " $\text{N-C}_2\text{-C}_6\text{alkanoylC}_2\text{-C}_6\text{aminoalkyl}$ " is unclear as to its metes and bounds, particularly as it depends from Claim 12, which is limited to a  $\text{C}_{1-12}$  alkyl group. The term " $\text{C}_{1-12}$  alkyl group", as explained using the definition on pages 14-15, refers to a hydrocarbon of one to twelve carbons in length containing only carbon and hydrogen. The term "optionally substituted" allows for substituents off the



Art Unit: 1652

carbon backbone, but not a nitrogen atom in the backbone as implied by  $N-C_2-C_6$ alkanoyl $C_2-C_6$ aminoalkyl and as required for using SNAC (Claim 15). Thus, all this nomenclature must be clarified considering the further limiting nature of dependent claims as well as organic chemistry. Clarification is required.

19. Claims 18-27, 47-48, and 50-55 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In the limitations of  $R_1$  and  $R_2$ , the phrase “**the** synthetic and biosynthetic amino acid residue side chains” (emphasis added) is unclear because the article ---the--- indicates particular residue side chains and none have been particularly defined. The Examiner suggests deletion of the “the” wherein ---any--- residue side chains will be the limitation. Clarification is required.

20. Claims 20 and 48 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In the limitations of the pH of the side chain, the phrase “about pH 7” is unclear as to its scope. Does “about” limit to  $\pm 1$  pH unit? Or  $\pm 2$  pH units? Or  $\pm 5$  pH units? The specification gives no indication of scope since pH values for side chains is not mentioned in the experiments so one of skill in the art would have to assume any side chain and, thus, any pH value from glutamate (acidic) to asparagine (basic) and then some considering non-native amino acid side chains. Thus, the ordinarily skilled artisan cannot ascertain the scope of the claims from any variability in the examples. The metes and bounds are not clear in the

Art Unit: 1652

claims, and the specification does not aid in the interpretation of the term "about". Clarification is required.

21. Claims 28-33 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In Claim 28,  $R_1$  and  $R_2$  are not defined, and their structure is, thus, unclear. Clarification is required.

22. Claims 31 and 33 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase "and the like" is wholly unclear as to the metes and bounds of the limitations of the non-peptidic SPACER. Clarification is required.

23. Claim 33 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The limitation of the spacer being non-peptidic is unclear wherein a functional group in the Markush list is glycine, an amino acid. Clarification is required.

24. Claims 34-55 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In Claim 34, the term "essentially" in the first step is unclear as to its metes and bounds. Can any cyclization take place without elongation and meet the limitations of the claim? If yes, then how much before the term "essentially" is no longer met? Clarification is required.

Art Unit: 1652

25. Claims 34-55 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In Claim 34, the "contacting" step is unclear because the substrate is contacted with a TE domain protein in the first step, and since heterodimer substrates can be formed in the first step, anything greater than 2 residues would meet the limitations of being the "elongated" substrate. Is there any difference in conditions other than length of the substrate? The specification does not discuss as much. Thus, the final step of Claim 34 is unclear. Clarification is required.

26. Claim 59 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In the first line, the phrase describing the limitation is "can be". It is unclear if this is a real limitation or not. Clarification is required. The Examiner suggests replacing the limitation with ---is--- for clarity.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

27. Claims 1-55 and 59 are rejected under 35 U.S.C. 112, first paragraph, written description, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the

Art Unit: 1652

application was filed, had possession of the claimed invention. The instant claims are directed to methods of cyclizing compounds wherein few structural limitations are imposed on said compounds with respect to the functional examples in the specification.

The Court of Appeals for the Federal Circuit has recently held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as be structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.*, 1997 U.S. App. LEXIS 18221, at \*23, quoting *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe a genus, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these.

In the instant specification, the majority of the substrates used in the cyclization reactions are short peptides (Examples 3-21) or depsipeptides (Examples 22-23). The example with compound 24 teaches using a peptide with a hydroxyl group at its N-terminus instead of the amine group. The examples with compounds 25-26 teach using an ethylglycolate spacer to substitute for some of the residues in the peptide. And finally the example with compound 27 teaches using a 3-hydroxybutanamide at the N-terminus of the peptide substrate. All the substrate examples have an SNAC functional group that is not encompassed in the "optionally substituted C<sub>1-12</sub> alkyl group of Claim 12, for example. Thus, no examples lack peptide residues

Art Unit: 1652

as part of the substrate, yet none of the instant claims require peptides as part of the substrate. No examples of using a substrate with an -SH nucleophile are taught. In its most general, the substrate is only required to have a nucleophile (any nucleophile) and an activated acyl group (any C=O next to an electron-loving atom). No correlation of structure of the substrate and function with all TE domains is described. Thus, the few examples describing the use of peptide substrates does not support the claimed genus so that one of skill in the art would be able to predict the structure of the substrates usable in the claims.

28. Claims 34-55 are rejected under 35 U.S.C. § 112, first paragraph, written description, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Although the genus of methods is discussed in the specification, there is no evidence that any representative species of such a large and varied genus, wherein the elongation step is repeated indefinitely, was in the possession of the inventors at the time of filing.

To satisfy the written description aspect of 35 U.S.C. § 112, first paragraph, for a claimed genus of molecules, it must be clear that: (1) the identifying characteristics of the claimed molecules have been disclosed, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these; and (2) a representative number of species within the genus must be disclosed. The specification does not disclose any representative species of the claimed methods. The single example that supports the elongation/cyclization method is found on pages 45-46, wherein a dimer is cyclized. In Claim 34, a dimer is formed in the first

Art Unit: 1652

elongation step; repetition would produce a product with two dimers that could then cyclize or continue oligomerizing. Thus, the example in the specification is distinct from the claimed methods.

29. Claims 1-55 and 59 are rejected under 35 U.S.C. § 112, first paragraph, scope of enablement, because the specification, while being enabling for methods using NRPS TE domains with particular substrates, does not reasonably provide enablement for methods using any PKS TE domains with any substrate or methods using NRPS TE domains with any substrate. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. The practice the methods to the full extent of their scope would require undue experimentation.

The factors to be considered in determining whether undue experimentation is required are summarized in *re Wands* 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir, 1988). The Court in *Wands* states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.'" (*Wands*, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (*Wands*, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the

Art Unit: 1652

relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

The instant specification describes TE domains as portions of polyketide synthases (PKSs) or non-ribosomal peptide synthetases (NRPS). The examples exclusively use NRPS TE domains; no PKS TE domains are used. The specification describes how excised TE domain a polyketide synthase, DEBS, does not promote cyclization (see specification page 3). No guidance is presented for the use of PKS TE domains, in particular for the substrates necessary for the use of PKS TE domains. The state of the prior art contradicts the claim that excised PKS TE domains promote cyclization. Thus, the predictability of using any substrate with an excised PKS TE domain is extremely low. For all these reasons, the instant claims are not enabled for using PKS TE domains.

In the instant specification, all examples except one utilize the excised TE domain protein from the tyrocidine NRPS (TycC); a single example using the excised TE domain protein from the surfactin synthetase is also described. The examples using TycC somewhat systematically utilize substrates varied on the particular *peptide* theme of substrates to determine where the substrate can be flexible and where it cannot. In the case of TycC, this is described as a straightforward process; however, this process using other excised TE NRPS domain proteins is wholly unpredictable since all NRPS substrates are distinct, except for their peptide nature. And the substrates usable in the claimed methods do not require any such peptide nature! Moreover, in some claims, the length of the substrates is infinite (see Claim 10, wherein the linker comprises **at least** 14 atoms). The nature of the art, in the absence of crystallography data on the

Art Unit: 1652

TE domain protein used in the methods, is directed trial-and-error at best to identify suitable substrates. To produce TE domain proteins that cyclize all the substrates in the claimed genus (or at least a significant number of them to include as few inoperative embodiments as possible) would require mutation of the proteins, which experimentation is wholly undescribed and unpredictable based on the instant disclosure. For all above reasons, the instant claims are not enabled to the full extent of their scope.

### ***Claim Rejections - 35 U.S.C. § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

30. Claims 1-8 and 11 are rejected under 35 U.S.C. § 102(a) as being anticipated by Trauger *et al.* (Peptide cyclization catalysed by the thioesterase domain of tyrocidine synthetase. Nature. Sept. 2000. 407:215-218). Trauger *et al.* is considered “by others” because inventors Burkart and Schwarzer are not authors. The instant claims are drawn to methods of cyclization using an activated thioester, peptide substrate that contains a nucleophile in an at least 90% aqueous solution of pH 7.0 using a TE domain protein.

Trauger *et al.* teach cyclizing SNAC peptides using an excised TE domain from the tyrocidine synthetase in an aqueous solution, pH 7.0 (see Abstract and “Assays”). Said aqueous solution is 100% water-based with no organic solvent component; Claim 4 is included in the rejection because the organic solvent need not be present if the solution is 100% aqueous.



Art Unit: 1652

The Examiner notes that other claims in the thioester species are excluded from the instant rejection due to the limitation of R as an optionally substituted C<sub>1-12</sub> alkyl group (see Claim 12), noted above in a rejection under 35 U.S.C. § 112, second paragraph, as not including SNAC. Moreover, although Trauger *et al.* teach elongation and cyclization, Claim 34 requires more than a dimer prior to cyclization as noted above in the rejection under 35 U.S.C. § 112, first paragraph, written description.

### *Conclusion*

31. Claims 1-55 and 59 are not allowed for the reasons identified in the numbered sections of this Office action. Applicants must respond to the objections/rejections in each of the numbered sections in this Office action to be fully responsive in prosecution.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kathleen M Kerr whose telephone number is (571) 272-0931. The examiner can normally be reached on Monday through Friday, from 9:00am to 6pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathupura Achutamurthy can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.



Kathleen M Kerr  
Examiner  
Art Unit 1652

January 23, 2004